IPAR

Public Assessment Report for a

Traditional Herbal Medicinal Product for Human Use

Name of Product: Urostemol Men capsules

TR1186/7/1

TR holder: Chefaro Ireland DAC

Date March 2016<DATE of last revision, month, year)< SPAN>

I INTRODUCTION

Specific provisions were introduced for traditional herbal medicinal products (THMPs) in accordance with the Traditional Herbal Medicinal Products Directive (2004/24/EC). The national regulations, the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 2007) which implement this Directive came into force on 23rd July 2007. Consequently the HPRA has established the Traditional Herbal Medicinal Products Registration Scheme.

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a Certificate of Traditional Use Registration for a specific traditional herbal medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of EC Directive 2001/83/EC, as amended by Directive 2004/27/EC and Directive 2004/24/EC. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the traditional herbal medicinal product for marketing in Ireland.

Based on the review of the data on quality, safety and traditional use, the HPRA has granted Chefaro Ireland Ltd a Certificate of Traditional Use Registration for Urostemol Men capsules. Each capsule contains 400 mg of pumpkin seed, crushed (*Cucurbita pepo* L. convar. *citrullina* I. Greb. var. *styriaca* I. Greb); 340 mg of pumpkin seed oil (*Cucurbita pepo* L. convar. *citrullina* I. Greb. var. *styriaca* I. Greb); 75 mg of extract (as dry extract) from saw palmetto fruit (*Serenoa repens* (Bartram) small) (7−13 : 1), extraction solvent ethanol 90% (m/m).

This application was submitted as a standard application according to Article 16c of Directive 2001/83/EC, as amended, as part of the Traditional Herbal Medicinal Product Registration Scheme.

The Summary of Product Characteristics (SmPC) for this traditional herbal medicinal product is available on the HPRA's website.

II QUALITY ASPECTS

This application is for Urostemol Men capsules. The active ingredients of Urostemol Men are pumpkin seed, pumpkin seed oil, and dry extract from saw palmetto fruit.

II.1 S.1 Herbal Substance

The specifications of the herbal substances (pumpkin seed and Saw Palmetto Fruit Ph. Eur.) are considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with the herbal substance specifications have been provided.

II.2 S.2 Herbal preparation

The herbal preparations are crushed pumpkin seed, pumpkin seed oil and dry extract from saw palmetto fruit. They are manufactured in accordance with the principles of good manufacturing practice (GMP).

The herbal preparation specifications are considered adequate to control the quality and meet current pharmacopoeial requirements. Batch analytical data demonstrating compliance with these specifications have been provided.

II.3 Medicinal product

P.1 Composition

The composition of the medicinal product is stated in sections 2 and 6.1 of the SmPC. A description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of GMP at suitably qualified manufacturing sites.

The manufacturing process involves standard operations only and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary Substances)*

All ingredients comply with the European Pharmacopoeia or are adequately controlled by the manufacturer’s specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for capsules, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the blister strip complies with EU legislation for use with foodstuffs.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Conclusion on quality

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Urostemol Men capsules.

III NON-CLINICAL ASPECTS

Urostemol Men is a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC as amended.

An expert report on safety has been provided which includes an appropriate review of the available literature.

No genotoxic potential was observed in the AMES test for this specific product formulation. No other new preclinical studies have been submitted. Given the type of application and limited data available, it is not possible to assess if the safety package for the phytochemical constituents of Urostemol Men are acceptable to the standards of today's GLP and safety testing requirements.

Overall the information presented demonstrating traditional use is considered to be acceptable and the lack of provision of a complete standard safety package is in line with the EMA 'Guideline on Non-clinical Documentation for Herbal Medicinal Products in Applications for Marketing Authorisation (bibliographical and mixed applications) and in Applications for Simplified Registration' (EMEA/HMPC/32116/05).

An environmental risk assessment is not required for herbal medicinal products according to guidance CPMP/SWP/4447/00.

IV CLINICAL ASPECTS

This is a national application submitted by Chefaro Ireland Ltd under Article 16c of Directive 2001/83/EC, as amended.

Urostemol Men is a traditional herbal medicinal product used for the relief of lower urinary tract symptoms in men related to an overactive bladder or bladder weakness, such as urgency to urinate, urinary incontinence or frequent urination day and night. This is exclusively based on long-standing use. Prior to treatment other serious conditions should be ruled out by a doctor.

IV.1 Clinical Efficacy

There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that the product is efficacious, the registration is based exclusively upon the longstanding use of Urostemol Men as a traditional herbal medicine and not upon data generated from clinical trials.

Article 16c1(c) of Directive 2001/83/EC requires the applicant to provide bibliographic or expert evidence to show that the medicinal product in question, or a corresponding product, has been in medicinal use throughout a period of at least 30 years, including at least 15 years within the Community. With regard to this traditional use data, the requirements of Article 16c1(c) have been met.

The efficacy of this traditional herbal medicinal product is plausible on the basis of long standing use and experience.

The indication proposed for Urostemol Men is in line with traditional indications recorded and hence, compatible with the requirements of the Traditional Herbal Medicinal Products Directive 2004/24/EC.

IV.2 Clinical Safety

In accordance with Article 16c1(d) the applicant has provided a bibliographic review of the safety data together with an expert report.

It is strongly advised that you see a doctor before taking this product as urinary symptoms may be due to a serious underlying condition which only your doctor can diagnose.

If symptoms persist beyond 4 weeks or worsen during use a qualified healthcare professional should be consulted.

Due to a lack of data, the safety of this product for long term use has not been established.

The use in children and adolescents under 18 years of age is not recommended, because lower urinary tract symptoms in these populations require medical supervision.

If symptoms such as pyrexia, spasms, haematuria, urinary retention, painful urination, loin pain, abdominal or back pain are present or develop during use, medical advice must be sought.

Urostemol Men should not be used by those allergic to the active substances, to other members of the Cucurbitaceae family (such as watermelon, courgettes etc.), or to any of the excipients listed in the SmPC.

Urostemol Men contains saw palmetto and the safety of saw palmetto has not been studied in patients with hepatic and/or renal impairment.

A few cases of suspected interactions between saw palmetto extract and warfarin have been reported. Increased INR-values have been described.

Due to the possible risk of saw palmetto extract enhancing the anticoagulant or antiplatelet effect, the combination of Urostemol Men with anticoagulant or antiplatelet medication should be used with caution.

There has been a case report of intra-operative haemorrhage associated with the use of saw palmetto. The prolonged bleeding time may have been a result of platelet dysfunction caused by cyclooxygenase inhibition by Saw palmetto. As a precaution Saw palmetto should be discontinued and the platelet function assessed prior to patients undergoing surgery.

The following adverse reactions have been commonly reported: mild gastrointestinal complaints (abdominal pain, dyspepsia, nausea, vomiting, stomach discomfort, dysphagia, oesophageal pain, diarrhoea and eructation).

Headache and hypersensitivity reactions (rash, urticaria, erythema, pruritus, oedema and anaphylactic shock) have also been reported, the frequency is not known.

In conclusion, this product proves not to be harmful in the specified conditions of use based on the review of safety data, expert report and additional data provided.

IV.3 Pharmacovigilance

It should be noted that in accordance with Article 16g of Directive 2001/83/EC, as amended, the pharmacovigilance

requirements described in Articles 101- 108 of Directive 2001/83/EC, as amended, also apply in respect of traditional herbal medicinal products.

V OVERALL CONCLUSIONS

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of Urostemol Men

The HPRA, on the basis of the data submitted, considered that Urostemol Men demonstrated adequate evidence of traditional use for the approved indication and no new preclinical or clinical safety concerns have been identified.

A certificate of traditional use for Urostemol Men is granted.